TABLE II.—*Cases of Leprosy seen in Recent Decades by British Dermatologists*

	Lepromatous and Mixed	Tuberculoïd	Neural	Type Doubtful	Totals
Former cases :					
1. Dead	16	—	7	—	23
2. Repatriated ..	6	—	7	—	13
3. Last seen over 10 years ago ..	3	—	7	1	11
Little-infective living neural and tuberculoïd :					
4. Last seen under 10 years ago ..	—	—	4	—	4
5. At present under observation ..	—	1	11	2	14
Infective living lepromatous cases :					
6. At present under observation ..	18	—	—	—	18
7. Last seen under 10 years ago ..	4	—	—	—	4
Totals	47	1	36	3	87

the more dangerous lepromatous or cutaneous cases. Those styled "mixed" are included under the more infective lepromatous type, as bacilli may be numerous.

In Table II, lines 1 to 3 show respectively those already dead, those repatriated, and those presumed to be dead or to have passed into a little-infective stage. Those in Category 3 were last heard of from ten to upwards of thirty years ago. The presumption of death after that period is considered justifiable in patients of the lepromatous type, for no fewer than eleven out of thirteen such patients regarding whom information is available had died within one to eight years of being first seen. The whole of the cases in lines 1 to 3 may thus be regarded as no longer of any danger to the community.

Lines 4 and 5 show little-infective neural cases, including one with tuberculoïd lesions. They are still alive, or presumed to be alive, because they were last seen less than ten years ago. In view of the fact above recorded, that no such case has been known to cause infection in this country, they present very little danger to the British community, although in rare instances abroad neural cases have been known to pass into a more infective type.

Lines 6 and 7 each show infective lepromatous cases, those in the former line being known to be alive and in this country, and those in the latter being presumed to be alive as they have been seen within the last ten years. They number eighteen and four respectively, giving a total of twenty-two; they require further consideration.

Living Conditions of Infective Lepromatous Cases

These are shown in Table III, which brings out the following points: Of the twenty-two, five were safely accommodated at the St. Giles Homes; of two more it is reported that one is "strictly segregated" and the other is also isolated at home, "keeping absolutely to himself

TABLE III.—*Conditions of Living of the Infective Lepromatous Cases*

Isolated at the St. Giles Homes in Essex	5
Isolated with careful precautions at home	2
Reached a quiescent little-infective stage	2
Seen at the Tropical Diseases Hospital	4
Under expert care and treatment	5
Conditions unsatisfactory	4

and taking every precaution against dissemination" of his disease; in two more the disease has reached a quiescent and little-infectious stage under treatment; four others were seen at the Hospital for Tropical Diseases, London, and will doubtless have received full instructions regarding the necessary precautions; and a further five are under the highly expert care and treatment of London specialists. In the remaining four the living conditions were not regarded as very satisfactory. The first was reported in

1929 to be residing in a flat with his wife and a young maid during an attack of leprotic fever. The second, a Eurasian subject, was living in the provinces unsegregated. The third was living five years ago with his wife and adult daughter, aged respectively 55 and 35. With these four exceptions the infective cases appear to be well cared for and of little danger to the British community.

Conclusions

We conclude from the above data that the present position is reassuring in view of the fact that nearly all the cases of the infective type are under expert care. Moreover, the danger of infection under the good hygienic conditions of Great Britain is much diminished by the fact that the great majority of the repatriated patients are of a social position that permits them to live under favourable sanitary arrangements and to avoid overcrowding. Further, many of them have reached an age when they are unlikely to come into close and prolonged contact with children, who are considered particularly susceptible. We are, however, of the opinion that all infective lepromatous patients who are not in a position to carry out effective home isolation with absolute prohibition of close contact with children should, so far as is possible, be accommodated at the St. Giles Homes. If necessary, Government funds should be made available for effecting this purpose.

CHEMOTHERAPY OF GONOCOCCAL INFECTIONS IN WOMEN AND CHILDREN

BY

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In the past two years the results of chemotherapy of gonococcal infections in the male have been fully reported, but comparatively little has been published on the chemotherapy of gonorrhoea in the female. In this paper are discussed the methods adopted and the results obtained in three series of cases: (1) gonorrhoea in adult women—104 cases, mostly out-patients; (2) gonococcal vulvovaginitis in children—twenty cases, all in-patients; (3) gonococcal ophthalmia in infants—twenty cases, all in-patients.

1. Gonorrhoea in Adult Women

Of the 104 cases treated, forty were early acute cases, twenty-seven subacute, and thirty-seven chronic. The majority of patients were from 20 to 35 years of age. Three had abscess of Bartholin's glands, two had acute salpingitis, and two had both syphilis and gonorrhoea.

During a preliminary trial period efforts were made to determine the best time to start chemotherapy, the most effective daily dosage, and the optimum length of treatment. In one group of acute cases the drug was withheld for the first week to allow development of some degree of natural immunity. In another group the drug was administered at once in a dosage of 2 grammes daily for ten to twelve days; while in a third group a smaller daily dosage was given for seven to ten days. The method which seemed to us to give the best results was the administration of one tablet (0.5 gramme) of sulphapyridine (M & B 693) four times daily after food for one

week, starting as soon as the diagnosis of gonorrhoea was made; and this was adopted as routine. In addition, local treatment was carried out, consisting of the application of 10 per cent. protargol to the urethra and cervix. This was given from the start daily until the onset of the menstrual period following cessation of the drug, and thereafter once or twice weekly for another month. For the next four weeks examination was made once weekly, and local treatment was applied only if discharge or congestion persisted.

Reactions to Sulphapyridine

Patients did not complain unduly of any ill effects, and in point of fact complaints were seldom elicited except after leading questions. Inquiry as to these side-effects was made as a precautionary measure against the unknown risks of giving such a potent drug to ambulant patients. The chief discomforts occurring were nausea (twenty-two cases), headache (nine cases), and drug rash (seven cases).

Nausea was reported on the third or fourth day of treatment, and was relieved in nineteen of the twenty-two cases by giving half a drachm of sodium bicarbonate along with the drug. In two of the three cases not so relieved a reduction in dosage to half a tablet six times a day overcame the nausea; but in the third case this measure failed, and the use of the drug had to be abandoned. Headache was synchronous in onset with the nausea, and it passed off spontaneously within forty-eight hours. It was never severe enough to require reduction of dosage or special measures for its relief.

Skin eruptions were few, and were mostly scarlatiniform. Generalized pruritus and oedema of the face were common accompaniments. The dermatitis began on the ninth day in every case. In two instances the rash appeared two days after the administration of the drug had ceased. In the others treatment had been continued for nine days, with a total dosage of 36 tablets (18 grammes). Invariably the condition called for no special treatment and cleared up rapidly on withdrawal of sulphapyridine. In one case, early in the series, marked herpes oris developed, and the drug was stopped. In the light of later experience it seems probable that the herpes was not caused by the sulphapyridine.

Results of Treatment of Gonorrhoea

Progress was noted by examination of daily smears from the urethra and cervix during administration of the drug, and of weekly smears up to the second menstrual period thereafter. Subsequently—that is, after cessation of local treatment—smears were examined after the three following menstrual periods. The standard of cure required was that all of these following the week of treatment with sulphapyridine should be negative. Nine cases of the series defaulted before observation had been completed, but eighty-three of the remaining ninety-five (87.4 per cent.) fulfilled these requirements—a highly satisfactory rate of cure. In twelve cases the result was unsatisfactory (Batchelor, Lees, Murrell, and Braine, 1938). A study of these twelve cases shows that: (1) inadequate dosage due to either intolerance or faulty attendance for treatment was responsible for the unsatisfactory result in four cases; (2) relapse occurred after local treatment had been missed for several weeks in one case; (3) there was no response whatsoever to the drug in three cases; (4) after being negative during the administration of the drug and remaining satisfactory for varying lengths of time the gonococcus reappeared in spite of local treatment in four cases.

The further treatment of the unsatisfactory cases was as follows:

1. In four another course of sulphapyridine was given with poor result.

2. In four a mixed gonococcal vaccine was used with good result. The vaccine employed was the St. Mary's mixed gonococcal vaccine; small doses, starting at 0.2 c.cm. and increasing gradually, being given twice weekly until a dose of 1 c.cm. was reached. This dose was repeated at weekly intervals for three weeks.

3. In one case which relapsed after a second course of sulphapyridine and mixed gonococcal vaccine, a course of albucid (*p*-aminobenzene-sulphonacetamide)—one tablet six times daily for one week, accompanied by a mixed vaccine twice weekly—led to a satisfactory result.

4. In the remainder of the cases local treatment only was employed.

Treatment of Gonococcal Complications

In these the effect of sulphapyridine was striking. It was found that the complications cleared up without any treatment other than administration of the drug. This was noted in the three cases of Bartholinian abscess and the two cases of acute salpingitis. In the former cases smears were negative within one week and the glands were palpable within two weeks from the beginning of treatment. In none of them was incision or aspiration of pus found necessary. In the cases of salpingitis symptoms and signs cleared up within four days of starting treatment, although the cervical smears remained positive until immediately after the next menstrual period. Thereafter the smears were negative.

In the series there were two cases in which the presence of a double infection was noted. A very interesting point arose with regard to the possible effect of the drug on the appearance of the primary sore. In one patient, on the first examination, gonorrhoea was found to be present, and there was also a vulval sore not resembling a hard chancre. Treatment with sulphapyridine was begun at the outset. Examination of the serum from the sore by dark-ground illumination at the first visit was negative, as was the Wassermann reaction. Subsequent daily examinations of serum from the sore by dark-ground illumination were negative, and yet she developed a W.R. ++ and a maculo-papular rash five weeks from her first visit.

The second patient was referred for examination through her husband, who had a primary sore and acute gonorrhoea. At her first visit cervical and urethral smears were positive for the gonococcus, but there was no evident sore and her Wassermann reaction was negative. Treatment with sulphapyridine was begun at once. She was examined very carefully at each subsequent visit, and a Wassermann test was made fortnightly, with negative result. No sore was evident at any time either on the vulva or the cervix, and yet her Wassermann reaction was ++ two months after her first visit. On experimental syphilis in animals sulphapyridine appears to have no inhibitory action, and it may well be that the drug was not responsible for the atypical character of the syphilitic infection in our two patients; but these cases at least serve to emphasize the necessity for late serological tests for syphilis in all female cases of gonorrhoea undergoing chemotherapy.

2. Gonococcal Vulvovaginitis

The dosage of sulphapyridine was dependent on the age and development of the child, varying from a quarter-tablet four times daily for one week in infants under 3 months to a half-tablet six times daily for one week in

the older girls. This was accompanied by daily vaginal swabbing with 10 per cent. protargol and the application of dermatol powder. The average duration of local treatment (in the beginning daily, and latterly weekly) was four months, while the limits were three months and nine months. The children remained well while the drug was administered, and no complaints were made.

The results in the twenty cases of the children's series were much less gratifying than in the adult group. Only eleven cases were classified as satisfactorily cured; seven cases were regarded as unsatisfactory and requiring further treatment. In three of these a second course of sulphapyridine gave a satisfactory result; in a fourth the third course was found effective; while in another two a mixed vaccine led to a cure (Brown, 1939). Our experience suggests the advisability of giving as a routine in all cases of gonococcal vulvovaginitis two courses of sulphapyridine separated by an interval of ten days or a fortnight.

3. Gonococcal Ophthalmia

In hospital twenty cases of gonococcal ophthalmia have been treated with sulphapyridine. The routine adopted was a quarter-tablet four times daily, given with sodium bicarbonate. This was supplemented by irrigation with normal saline, the frequency of this depending on the severity of the case, the average being four-hourly. Smears from all the cases were negative within four days, even in two which had failed to respond to local treatment and protein shock. In none of the cases was there any relapse: after the smears became negative they remained so. Tablets were discontinued forty-eight hours after the smears became negative. A total dosage of 3 grammes sufficed in every case. Given crushed in milk to which a pinch of sodium bicarbonate was added, the drug caused no signs of intolerance.

Discussion

A general survey of the effects of sulphapyridine brought out several points of interest:

1. The effect of the drug does not appear to be dependent on the particular strain of the organism, as was believed at an earlier stage. This point was illustrated in three sets of patients: (a) Where husband and wife received treatment at the same time, the husband having infected his wife and both seeking treatment immediately. The response in the case of the wife was very satisfactory, but the husband's case was classified as a failure at the male clinic, although he showed no intolerance to the drug and had had a very adequate dosage. (b) Two instances where mother and child received treatment at the same time. In one the child responded and the mother did not; in the other the mother responded while the child did not.

2. Acute and chronic cases responded equally well to the treatment. Of the thirty-seven chronic cases four were failures, while a similar number of failures were found among the forty acute cases.

3. Response to the treatment is rapid, smears becoming negative between the second and fifth days. Continued administration beyond one week did not appear to have any added advantage. Where rapid improvement failed to show itself there was little likelihood of subsequent response. Prolongation of treatment beyond the period indicated increased the probability of ill effects without any added benefit. This is illustrated by the skin manifestations. Of the seven cases four occurred where the drug was continued beyond one week.

4. In the case of the children it was found that although they were in hospital the results were sometimes very disappointing. The reason for this appeared to be that the interval between the last dose at night and the first in the morning was too long. The results were much improved when the last dose was given later at night, thus maintaining a more uniform concentration of the drug in the blood (Marshall, Cutting, and Emerson, 1938).

5. The persistence of the positive cervical smear in the case of salpingitis suggested that the giving of the course of treatment during the menstrual period might lead to even better results, especially in the chronic cases.

Summary

In the treatment of gonorrhoea in the adult female the administration of sulphapyridine is a great advance on the older methods. In the present series 87.4 per cent. of the cases were cured in a very much shorter period than was previously possible.

In children suffering from vulvovaginitis the results are less encouraging.

With the dosage used the ill effects of the drug are infrequent and of no great severity.

In the treatment of complications of the infection in adults no measures other than the administration of sulphapyridine are necessary.

No failures have occurred in the treatment of gonococcal ophthalmia with sulphapyridine.

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TUBERCULOSIS OF THE KNEE A FOLLOW-UP INVESTIGATION OF OLD CASES

BY

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An investigation of old cases of tuberculosis of the knee treated at the Robert Jones and Agnes Hunt Orthopaedic Hospital was made for presentation to the British Orthopaedic Association at Oswestry in May, 1939, and a summary of the results obtained has been included in Professor Girdlestone's book *Tuberculosis of Bone and Joint*, recently published. Owing to the tracing of a few additional patients the figures in this paper differ slightly from those originally presented.

The object of the investigation was to follow up old cases only, and it was decided that no patient with a history of less than five years should be included. The period 1920-34 was chosen, and all the cases investigated were first admitted to the hospital during that period, though the onset of the disease in many was prior to that time. Between 1920 and 1934 inclusive 2,922 patients suffering from bone and joint tuberculosis were admitted to the hospital, and included in this number were 322 cases which were diagnosed as tuberculosis of the knee. This represents an incidence of 11 per cent. The task of tracing all these patients, most of whom were scattered throughout the length and breadth of the country, was